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Original research article

# Hyperdense middle cerebral artery sign as the only radiological manifestation of hyperacute ischemic stroke in computed tomography

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ABSTRACT

*Objectives:* The main aim of the study was to find the effect of hyperdense middle cerebral artery sign (HMCAS), as the only admission computed tomography (CT) manifestation of ischemic stroke involving middle cerebral artery (MCA) region, on the extent of stroke measured by Alberta Stroke Program Early CT score (ASPECTS) in the follow-up CT. The secondary aim was to determine the correlation between length of hyperdense MCA segment on admission CT and ASPECTS in follow-up CT.

*Methods:* The group analyzed consisted of 118 patients with ischemic MCA region stroke, with no early signs of brain tissue ischemia on admission CT, but infarcts confirmed in follow-up CT, with extent evaluated using ASPECTS. For the subgroups: 66 patients with HMCAS present and 52 with HMCAS absent, median ASPECTS values were compared. In the subgroup with HMCAS present, length of hyperdense segment was measured and correlation with ASPECTS was determined.

*Results:* The median ASPECTS 6 (min. 0, max. 9) in the subgroup with HMCAS present was significantly lower, compared to the score 8.5 (min. 0, max. 9) in the subgroup with HMCAS absent. Moderate correlation between the length of hyperdense segment and ASPECTS was found ($R = -0.45$).

*Conclusion:* In patients with ischemic stroke involving MCA region and no early signs of brain tissue ischemia on the admission CT, HMCAS is associated with significantly lower ASPECTS in the follow-up CT. There is moderate correlation between the length of hyperdense MCA segment and ASPECTS.



## 1. Introduction

Magnetic Resonance (MR) Diffusion weighted imaging (DWI) may show increased signal in ischemic brain tissue even a few minutes after arterial occlusion [1–3].

However, in spite of increasingly better availability of MR, non-contrast computed tomography (CT) brain examination remains the basic imaging modality in patients with acute ischemic brain stroke [4–6]. The procedure is fast, inexpensive and widely available. The aims of CT in patients with clinical symptoms of stroke are: to exclude intracranial pathologies

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mimicking stroke such as tumor, to exclude intracranial hemorrhage precluding thrombolytic therapy and to look for early features of stroke.

In the first 3 h after symptom onset (hyperacute phase), brain tissue assessment in CT may show loss of gray-white matter differentiation, manifesting as loss of distinction among the nuclei of the basal ganglia (lenticular obscuration) or as blending of the densities of the cortex and underlying white matter in the insula (insular ribbon sign) and over the convexities (cortical ribbon sign), as well as cortical hypodensity and parenchymal swelling resulting in gyral effacement.

However, the ability of observers to detect these early infarct signs is limited and occurs in ≤67% of cases imaged within 3 h [6]. Detection is influenced by the size of ischemic region, severity of ischemia, and the delay from symptom onset. Sensitivity of detection may be increased with the use of a structured scoring system such as the Alberta Stroke Program Early CT Score (ASPECTS) or the CT Summit Criteria [7,8] as well as the use of dedicated "stroke CT window" [9].

Aside from brain parenchyma abnormalities, in some patients it is also possible to detect in CT a hyperdense segment of a vessel, representing direct imaging of the intravascular thrombus. It may be the earliest and only visible CT sign of ischemic stroke, especially. Although this can be seen in any vessel, it is most often observed in the middle cerebral artery (MCA) as hyperdense middle cerebral artery sign (HMCAS).

Increased attenuation may be visible in a long segment of MCA, especially the proximal portion or may be limited to a very short segment, usually distally, as an MCA dot sign.

The specificity of HMCAS is almost 100%, but the sensitivity is much lower – HMCAS is seen in only one third to one half of cases of angiographically proven thromboses [10,11].

It is very important for radiologists to recognize this sign, because it may help to save the patient in the time window for thrombolysis (4.5 h from stroke onset to rtPA treatment [4]).

There are only occasional reports of a hyperdense MCA sign seen in herpes simplex virus (HSV) encephalitis [12]. The other causes of false positive results are high haematocrit and atherosclerotic disease, especially with assymetric calcifications.

In histopathological studies the thrombus composition may be categorized into early phase (RBC – Red Blood Cell Count dominant and RBC proportion equal to fibrin) and late phase (fibrin dominant and organized fibrin). Hyperdense artery sign on CT is more commonly seen in RBC dominant or RBC proportion equal to fibrin compositions [13,14].

The main aim of the study was to find the effect of HMCAS present in patients with hyperacute cerebral ischemic stroke involving MCA region and no other early signs of brain tissue ischemia on the admission CT on the extent of stroke as measured by ASPECTS in the follow-up CT.

The secondary aim was to find out whether there is any correlation between the length of hyperdense MCA segment on the admission CT and ASPECTS in the follow-up CT.

## 2. Material and methods

From among all the patients with cerebral ischemic stroke involving MCA region, diagnosed and treated in the University Hospital in Cracow in the years 2011–2015, the cases were retrospectively selected with no early signs of brain tissue ischemia (hypodense areas/swelling of the gyri/loss of gray-white differentiation) visible on the admission CT, but with infarcts confirmed on the follow-up CT – Fig. 1.

The group analyzed consisted of 118 patients – 59 females and 59 males, aged 38–97 years (mean 72 years, SD 11.8 years). In 63 (53%) patients stroke involved the left MCA region, whereas in 55 (47%) patients – the right MCA region.

Non-contrast CT brain examinations were performed using 2.5 mm or 3 mm slices, 120–130 kV, 102–342 mAs.

The follow-up non-contrast CT examinations were performed within the mean time interval of 2 days (0–9 days) after the admission CT examinations.

The extent of ischemic changes on all the follow-up CT examinations was evaluated using Alberta Stroke Program Early CT score (ASPECTS). The assessment was performed independently by 2 trained radiologists (15 and 10 years' practice in stroke imaging, respectively) and the final ASPECTS was calculated as the mean of the 2 values obtained.

Then the whole group of 118 patients was divided into two subgroups depending on the presence of HMCAS on the admission CT examinations.

The subgroup with HMCAS present consisted of 66 patients (56%) – 34 females and 32 males, aged 39–97 years (mean 74 years, SD 10.9 years). The follow-up CT examinations in that subgroup were performed within the mean time of 2 days (0–5 days) after the admission CT examinations.

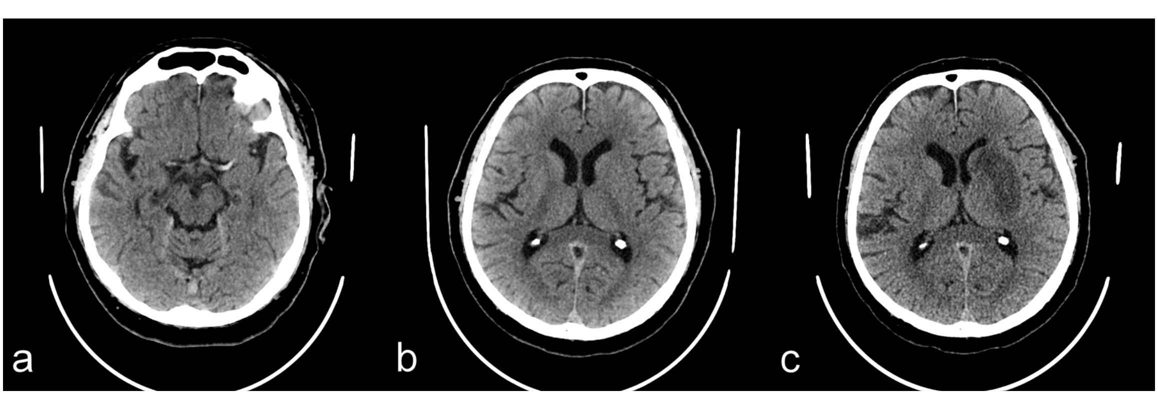


**Fig. 1 – (a) Admission CT – HMCAS, (b) admission CT – no early signs of brain tissue ischemia, (c) next-day follow-up CT – infarct confirmed.**

The subgroup with HMCAS absent consisted of 52 (44%) patients – 25 females and 27 males, aged 38–91 years (mean 70 years, SD 12.8 years). The follow-up CT examinations in that subgroup were performed within the mean time of 2 days (0–9 days) after the admission CT examinations.

The values of median ASPECTS were calculated in both the subgroups and then compared using the Mann–Whitney test because of ordinal scale of the data. The Shapiro–Wilk test was used to assess agreement between the distribution of a feature and theoretical normal distribution.

In the subgroup with HMCAS present, additionally the length of hyperdense segment was measured on CT images. The measurements were performed twice and the final length was calculated as the mean of the 2 values obtained.

The correlation between the length of hyperdense segment and ASPECTS was determined in that subgroup, based on Spearman rank correlation coefficient.

The result was considered significant if the calculated $p$-value was lower than significance level $\alpha = 0.05$. The statistical calculation was made by R software version 3.3.1 (www.r-project.org).

## 3. Results

In the whole group of 118 patients examined the median ASPECTS was 7 (minimum 0, maximum 9, lower quartile 5, upper quartile 9).

In the subgroup of 66 patients with HMCAS present the median ASPECTS was 6 (minimum 0, maximum 9, lower quartile 4, upper quartile 7.75).

In the subgroup of 52 patients with HMCAS absent the median ASPECTS was 8.5 (minimum 0, maximum 9, lower quartile 7, upper quartile 9).

The difference in median of ASPECTS scores between both subgroups was considered as statistically significant ($W = 2513.5$, $p < 0.001$) – Fig. 2.

In the subgroup with HMCAS present, the median length of hyperdense segment was 13 mm (minimum 3 mm, maximum 59 mm, lower quartile 8 mm, upper quartile 23 mm). Moderate correlation between the length of hyperdense segment and ASPECTS was found ($R = -0.45$, $p < 0.001$) – Fig. 3.

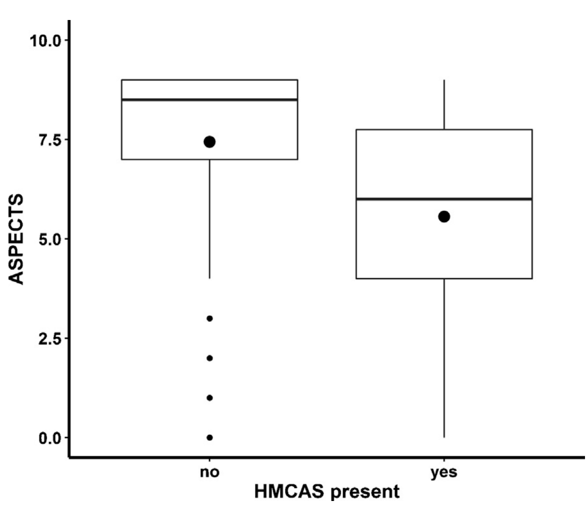


**Fig. 2 – Boxplot of ASPECTS scores depending on the presence of HMCAS. Dots represent the mean values.**

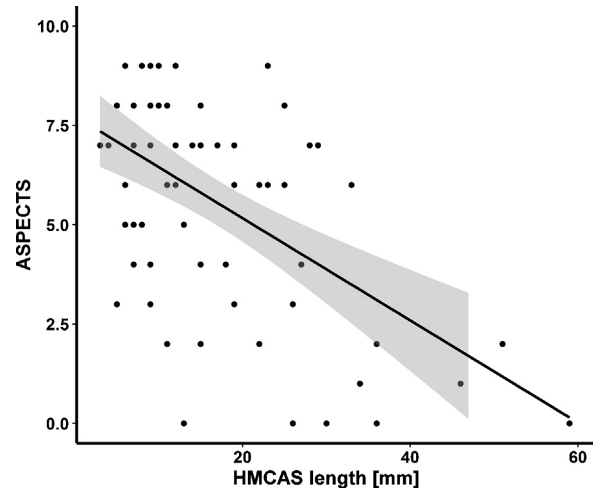


**Fig. 3 – Plot diagram: length of hyperdense MCA segment vs. ASPECTS score in the group of patients with presence of HMCAS. The solid line represents the regression line with the 95% confidence interval.**

All the cases with the length of hyperdense MCA segment > 25 mm resulted in ASPECTS < 8.

However, the group of the cases with the length of hyperdense MCA segment <10 mm included ASPECTS from 3 to 9.

## 4. Discussion

HMCAS is typically associated with a poorer clinical outcome, larger volume strokes, and more severe neurological deficits [10,15–18].

In many studies concerning a large group of patients treated with intravenous thrombolysis [18,19] higher stroke severity measured by National Institutes of Health Stroke Scale (NIHSS) was found in patients presenting HMCAS on baseline CT images.

Abul-Kasim [15] measured ASPECTS in MCA-stroke patients treated with intravenous thrombolysis, on CT images obtained 24 h after treatment. In the subgroup of patients with hyperdense MCA sign present on baseline CT images, significantly lower mean ASPECTS was found ($4 \pm 2$), compared to the subgroup of patients with hyperdense MCA sign absent ($8 \pm 2$). Thus the difference between the groups was even greater than that in our results.

Moreover, Paliwal [20] and Kharitonova [21] proved that persistence of hyperdense MCA sign on the follow-up CT in ischemic stroke patients treated with intravenous thrombolysis was an early predictor of poor functional outcome.

The length of hyperdense MCA segment correlates with the final outcome and the effects of treatment. Shobha [22] found that in a subgroup of acute stroke patients with HMCAS on baseline CT, treated with intravenous thrombolysis, the rate of disappearance varied depending on the baseline HMCAS length. Short-length HMCAS (<10 mm) disappeared in 85.7%, medium-length HMCAS (10–20 mm) – in 37.5% and long-length HMCAS (>20 mm) disappeared in none of the cases.

Similarly to our results, long hyperdense MCA segment is generally associated with significantly worse outcome.

Not only the length of hyperdense MCA segment, but also the location of the thrombus in the proximal or distal part of the vessel is important for the prognosis. Li [23] showed that poor neurological recovery post intravenous thrombolysis was confined to proximal HMCAS cases, contrary to distal HMCAS cases. Similarly, Man [24] found that proximal HMCAS predicts unfavorable outcome of intraarterial thrombectomy for acute stroke.

Hemorrhagic transformation is an infrequent but very serious complication of ischemic stroke treatment. Zou [25] concluded that HMCAS is associated with increased risk of hemorrhagic transformation after intravenous thrombolysis for patients with acute ischemic stroke.

One of the greatest problems concerning detection an assessment of hyperdense MCA sign on routine non-contrast CT examinations is a large slice thickness, reaching 5 mm, compared to the MCA diameter of 2–3 mm. It may result in partial volume effects blurring the intraluminal hyperdensity and lowering HMCAS detection sensitivity. Therefore, some authors suggest using thin slices of about 1 mm for the assessment of non-contrast CT examinations performed using multidetector CT scanners in stroke patients, which may considerably increase the sensitivity [26–28]. In our study we used slice thickness of 2.5–3 mm, comparable to the MCA diameter.

## 5. Conclusions

1. In patients with cerebral ischemic stroke involving MCA region and no early signs of brain tissue ischemia on the admission CT, HMCAS is associated with significantly lower ASPECTS in the follow up CT.
2. There is moderate correlation between the length of hyperdense MCA segment and ASPECTS.
3. Long hyperdense MCA segment is generally associated with a large area of brain tissue damage; however, short hyperdense MCA segment does not exclude large area of brain tissue damage.

## Conflict of interest

None declared.

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## Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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